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Predictors of Surgical Intervention in Neonates with Necrotizing Enterocolitis: A Retrospective Study

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ABSTRACT

Background: Necrotizing enterocolitis (NEC) is a severe gastrointestinal emergency in neonates with high death and morbidity.

Aim: This study aimed to recognize demographic, laboratory, and clinical predictors related to the need for surgical management in neonates with NEC.

Methods: This retrospective observational study was conducted on 200 patients over a three-year period in a tertiary neonatal intensive care unit. Neonates diagnosed with NEC (Bell's stage II or III) were included and divided into surgical and conservative management groups.

Results: A total of 200 neonates with NEC have been involved; 45 required surgical intervention, and 155 were managed conservatively. Neonates in the surgical group had significantly lower gestational age and birth weight (p under 0.001). Severe clinical features, including abdominal distension, abdominal rigidity, weak bowel sounds, poor mental reaction, tachycardia, and advanced Bell's stage, were significantly more prevalent in the surgical group (p below 0.05). Multivariate analysis recognized CRP and lactate as independent predictors of surgical intervention, while higher gestational age, absolute lymphocyte count, and white blood cell count were protective. ROC analysis showed good predictive accuracy for CRP (AUC = 0.792).

Conclusion: Prematurity, low birth weight, severe clinical presentation, and elevated inflammatory and metabolic markers are strongly associated with surgical NEC. CRP, in particular, is a reliable predictor and can aid in early recognition of high-risk neonates, facilitating timely surgical decision-making and improved outcomes.

KEYWORDS: Necrotizing enterocolitis; Surgical intervention; C-reactive protein; Neonates.

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INTRODUCTION

NEC is a prevalent and severe illness in newborns. The death rate of NEC varies from twenty percent to thirty percent. About 25 to 50 percent of these cases require surgery. Surgical NEC has been related to significantly higher death and morbidity rates compared to medical NEC **(1)**.

Around ten percent of NEC cases appear in full-term infants, who frequently exhibit comorbidities like congenital heart disease, chromosomal anomalies, gastrointestinal anomalies, or sepsis. Preterm and term babies demonstrate significant differences in clinical manifestations and illness progression, with term babies demonstrating reduced rates of operation, emphasizing the requirement for tailored treatment options **(2)**.

Throughout the assessment of a possible surgical patient, it is crucial to avoid intestinal gangrene, as it may lead to bowel loss and consequent long-term nutrition and developmental sequelae. through several attempts to determine which babies would benefit from an operation, an accurate indication of the required of surgery in these complex cases has yet to be developed **(3)**.

Hypothermia, absent bowel sounds, WBC > 20 × 109/L or < 5 × 109/L, CRP > 50 mg/L, pneumatosis intestinalis, and ascites were independent risk factors for operation **(4)**.

The current research aimed to assess the predictors of operation in newborns with necrotizing enterocolitis.

PATIENTS AND METHODS

This retrospective observational research was conducted on 200 newborns diagnosed with NEC throughout the research duration, recognized through medical record review at a tertiary neonatal intensive care unit (NICU) over a 3-year study interval.

Inclusion criteria: Neonates of any gestational age or birth weight with a validated diagnosis of NEC (Bell's stage II or III) were included.

Exclusion criteria: Neonates with congenital gastrointestinal anomalies, chromosomal abnormalities, incomplete medical records, or those who underwent surgery for indications other than NEC.

Patients have been categorized into 2 groups according to management approach: Surgical group: 45 neonates who required surgery for NEC (Bell's stage IIIA or IIIB) and Conservative group: 155 neonates managed medically without surgical intervention (Bell's stage II).

METHODS

All patients were subjected to the following:

Data collection

The following data were retrospectively collected from medical records:

Demographic and perinatal data: sex, gestational age, birth weight at diagnosis, and age at diagnosis. **Clinical characteristics:** fever, poor mental reaction, emesis, gross bloody stool, apnea, abdominal distension, abdominal rigidity, bowel sounds, gastric retention, colored gastric aspirate, tachycardia, and Bell's stage and **laboratory findings:** Complete blood count (absolute neutrophil count, white blood cell count, hemoglobin, absolute lymphocyte count, and platelet count), C-reactive protein (CRP), arterial blood gas parameters (pH and bicarbonate), and serum lactate levels. Laboratory data have been gained at the time of NEC diagnosis or at clinical deterioration requiring surgical evaluation.

Outcome Measures

The 1^{ry} outcome was the requirement for surgical intervention. 2^{ry} outcomes comprised identification of independent predictors of surgical NEC and assessment of the diagnostic performance of laboratory biomarkers.

Statistical Analysis

Statistical analysis has been carried out applying GraphPad Prism (version 8; GraphPad Software, United States of America). Continuous parameters have been represented as mean ± standard deviation (SD), and categorical parameters as percentages and frequencies. Comparisons among groups have been carried out utilizing the chi-square test for categorical parameters and the independent t-test for continuous parameters. Multivariate logistic regression analysis has been used to determine independent predictors of surgical intervention, with results expressed as odds ratios (ORs) and 95% confidence intervals (CIs). Receiver operating characteristic (ROC) curve analysis was applied to evaluate the predictive accuracy of significant biomarkers. A p-value below 0.05 has been regarded statistically significant.

RESULTS

Table (1): Baseline demographic and perinatal features among studied groups.

		Surgical group)N=45(		Conservative group (N=155)		Test value (X^2)	P-value
		No.	%	No.	%		
Gender	Male	23	51.1	87	56.1	0.355	0.551
	Female	22	48.9	68	43.9		
Gestational age	<32 weeks	14	31.1	21	13.5	14.928	**<0.001**
	32–36 weeks	21	46.7	52	33.5		
	≥37 weeks	10	22.2	82	52.9		
Birth weight at diagnosis	<1500 g	8	17.8	13	8.4	13.843	**<0.001**
	1500–2500 g	26	57.8	56	36.1		
	>2500 g	11	24.4	86	55.5		
Age at diagnosis	<7 days	17	37.8	32	20.6	5.584	0.06
	7–13 days	10	22.2	41	26.5		
	≥14 days	18	40.0	82	52.9		

Gestational age and birth weight were significantly lower in the surgical group ($p < 0.001$ for both), indicating that low birth weight and prematurity are major risk factors for surgical NEC. Sex illustrated non-significant variance among groups (p equal

0.551). Age at diagnosis showed a trend toward earlier presentation in the surgical group nevertheless, didn't reach statistical significance (p equal 0.06). (Table 1)

Table (2): Clinical features among studied groups.

		Surgical group)N=45(		Conservative group (N=155)		Test value (X^2)	P-value
		No.	%	No.	%		
Fever		10	22.2%	15	9.7%	5.018	**0.03**
Poor mental reaction		27	60.0%	41	26.5%	17.492	**<0.001**
Emesis		11	24.4%	41	26.5%	0.073	0.740
Gross bloody stool		22	48.9%	91	58.7%	1.369	0.232
Apnea		5	11.1%	13	8.4%	0.316	0.574
Abdominal distension		45	100%	88	56.8%	29.251	**<0.001**
Rigid abdomen		26	57.8%	20	12.9%	39.655	**<0.001**
Weak bowel sounds		37	82.2%	52	33.5%	33.454	**<0.001**
Gastric retention		6	13.3%	18	11.6%	0.098	0.754
Colored gastric aspirate		5	11.1%	15	9.7%	0.08	0.777
Tachycardia		12	26.7%	9	5.8%	16.149	**<0.001**
Bell's stage	II	0	0%	151	97.4%	179.526	**<0.001**
	IIIA	20	44.4%	3	1.9%		
	IIIB	25	55.6%	1	0.7%		

Poor mental reaction, fever, rigid abdomen, abdominal distension, weak bowel sounds, and tachycardia were significantly more frequent in the surgical group ($p < 0.05$), reflecting more severe clinical presentation. Bell's stage was strongly associated with surgical intervention, with all surgical cases classified as stage III, whereas nearly all conservative cases were stage II ($p < 0.001$). Other symptoms, including emesis, bloody stool, apnea, and gastric aspirate, illustrated non-significant variances among groups. (Table 2)

Table (3): Laboratory findings among studied groups.

		Surgical group (N=45)	Conservative group (N=155)	Test value (T)	P-value
White blood cell (×10⁹/L)	**Mean± SD**	6.1 ± 3.2	11.2 ± 4.8	6.7019	**<0.001**
	Range	1.9 – 14.3	5.1 – 22.4		
Absolute neutrophils (×10⁹/L)	**Mean± SD**	5.4 ± 2.6	2.9 ± 1.8	7.3615	**<0.001**
	Range	1.6 – 12.3	0.9 – 8.4		
Absolute lymphocytes (×10⁹/L)	**Mean± SD**	1.6 ± 0.8	3.4 ± 1.6	7.2778	**<0.001**
	Range	0.5 – 4.2	1.1 – 7.2		
Neutrophil-to-	**Mean± SD**	2.3 ± 1.1	1.6 ± 0.9	1.2531	0.352

lymphocyte ratio	**Range**	0.8 – 6.5	0.4 – 4.1		
Hemoglobin (g/dL)	**Mean± SD**	11.83 ± 2.14	13.85 ± 2.21	5.4356	**<0.001**
	Range	7.2 – 15.8	9.8 – 18.2		
Platelets (×10⁹/L)	**Mean± SD**	134 ± 72	276 ± 96	9.1936	**<0.001**
	Range	28 – 310	122 – 518		
CRP	**Mean± SD**	77 ± 42.7	16.9 ± 15.8	14.433	**<0.001**
	Range	14 – 168	1 – 82		
Blood pH	**Mean± SD**	7.33 ± 0.10	7.40 ± 0.08	3.4252	**0.001**
	Range	7.02 – 7.47	7.21 – 7.52		
Lactate (mmol/L)	**Mean± SD**	3.39 ± 1.35	1.96 ± 0.75	9.311	**<0.001**
	Range	0.5 – 7.8	0.1 – 3.9		
Bicarbonate (mmol/L)	**Mean± SD**	19.6 ± 4.6	21.5 ± 3.7	1.54	0.13
	Range	9.8 – 28.3	12.4 – 30.1		

The surgical group showed significantly lower lymphocyte count, white blood cell count, hemoglobin, platelet count, and blood pH, and significantly higher neutrophil count, CRP, and lactate levels compared with the conservative group ($p < 0.001$), indicating more severe systemic inflammation and metabolic derangement among neonates requiring surgery. Neutrophil-to-lymphocyte ratio and bicarbonate levels didn't differ significantly among the 2 groups (p above 0.05). (Table 3)

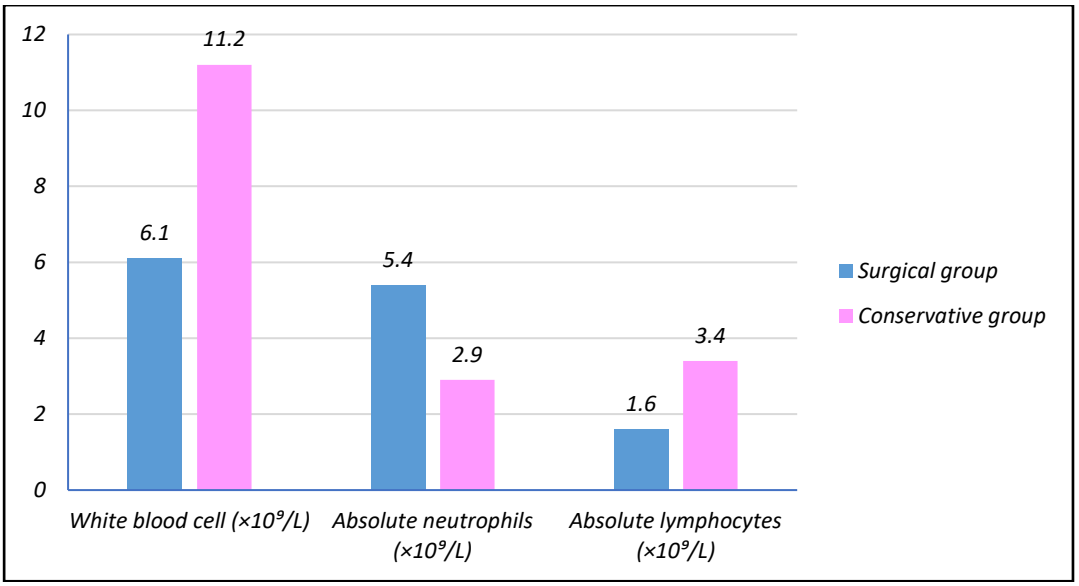

Figure (1): Laboratory findings among studied groups.

Table (4): Regression analysis for predictors of surgical Intervention in Newborns had NEC.

	β	OR	P value	95% CI
CRP (mg/L)	0.028	1.029	<0.001	1.008 – 1.041
White blood cell count (×10⁹/L)	−0.176	0.839	0.009	0.708 – 0.938
Absolute lymphocyte count (×10⁹/L)	−0.501	0.606	0.039	0.357 – 0.967
Lactate (mmol/L)	0.331	1.392	0.021	1.060 – 1.892
Gestational age (weeks)	−0.672	0.228	0.04	0.047 – 0.832

In multivariate analysis, higher CRP and lactate levels were independent predictors of surgical intervention, while higher absolute

lymphocyte count, white blood cell count, and greater gestational age were protective factors against surgery. These findings indicate that severe systemic inflammation, metabolic acidosis, and prematurity significantly increase the likelihood of needing surgical management in newborns who have NEC. (Table 4)

Table (5): ROC curve for predictors of surgical Intervention in Newborns had NEC.

	AUC	Cut-off value	Sensitivity	Specificity
CRP (mg/L)	0.792	19.2	77%	82%
Lactate (mmol/L)	0.651	1.32	88%	37%

CRP demonstrated good discriminative ability for predicting surgical NEC (AUC = 0.792), with high specificity (82%) at a cut-off value of 19.2 mg/L. Lactate showed high sensitivity (88%) but poor specificity (37%), indicating that it is useful for ruling out severe disease but less accurate for confirming the need for surgery. (Table 5)

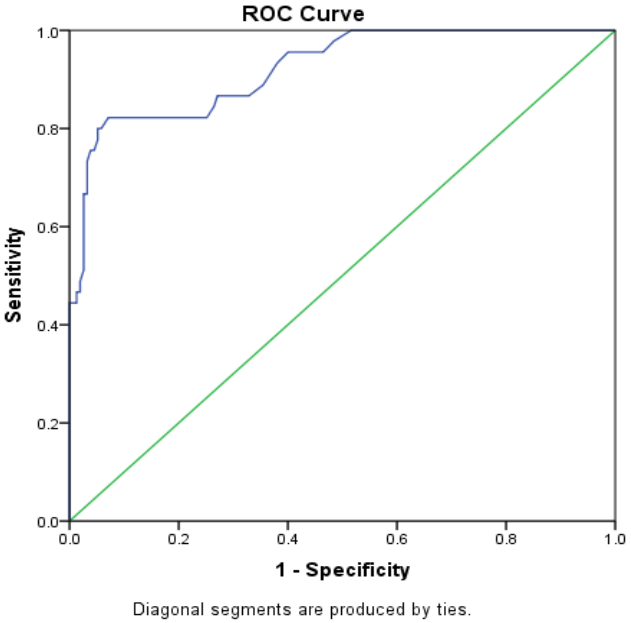

Figure (2): ROC curve for CRP of surgery in Newborns had NEC.

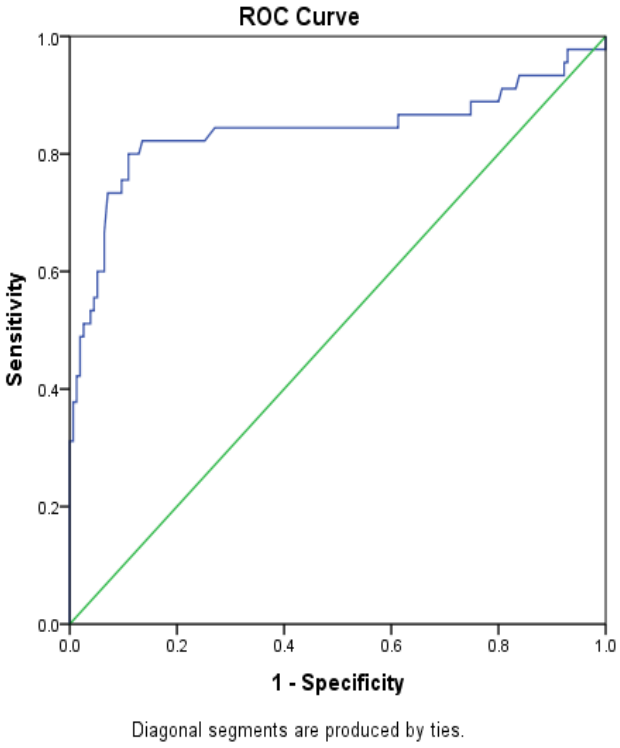

Figure (3): ROC curve for lactate of surgery in Newborns had NEC.

DISCUSSION

Regarding demographic and perinatal characteristics, there was no significant variance in gender among groups (P equal 0.551). In contrast, lower gestational age and birth weight were significantly related to surgical intervention (P below 0.001), with more preterm and lower-birth-weight newborns in the surgical group. Age at diagnosis showed an insignificant trend toward earlier presentation in surgically treated cases. Overall, prematurity and low birth weight appear to be key predictors of surgical NEC.

In agreement with **Yu et al.**, **(5)** who analyzed the features of neonatal necrotizing enterocolitis and objectives to recognize the risk factors for operation in necrotizing enterocolitis. They revealed that the gestation age (p equal 0.001) and weight at diagnosis (p equal 0.002) among the surgical group and the conservative group were significantly different. The age and gender at diagnosis weren't various among the 2 groups (all p over 0.05).

Similarly, it is consistent with **El Manouni El Hassani et al.**, **(6)** who aimed to recognize that clinical, perinatal, and laboratory variables are related to raised risk for operation in premature babies who had NEC. They reported that gestational age (GA) (p-value equal 0.001) and birth weight (p-value equal 0.015) were inversely related to the development of surgical NEC (sNEC).

In the present study, poor mental reaction, fever, abdominal distension, rigid abdomen, weak bowel sounds, and tachycardia were significantly more widespread in the surgical group (P below 0.05), indicating more severe disease. Other symptoms showed no significant differences. Bell's stage was strongly related to surgery, with all surgical cases classified as stage III compared with mostly stage II in the conservative group (P under 0.001), highlighting advanced disease severity as a key predictor of surgical intervention in NEC.

The outcomes were consistent with **Yu et al., (5)** who stated that cases in the surgical group exhibited a greater percentage of fever (p equal 0.025), diminished mental reaction (p below 0.001), pneumoperitoneum (p under 0.001), rigid muscle (p below 0.001), reduced bowel sound (p below 0.001), a high stage of Bell's stage (p under 0.001), and an elevated rate of moderate bacterial invasion compared to the conservative group. Non-significant variance has been observed in the existence of apnea, emesis, gross bloody stool, gastric retention, as well as colored beverage on gastric returns following gastric tube replacement among the 2 groups.

Similarly, in agreement with **Shang et al.**, **(7)** who explored early clinical predictive factors and surgical indications for neonatal NEC to enhance the prognosis of affected babies. Significant variances have been noticed among the surgical and non-surgical groups for fever, absent bowel sounds, and poor response (P below 0.05).

The current findings as regards laboratory data observed that those requiring surgery illustrated significantly lower lymphocyte counts and white blood cell, hemoglobin, platelet, and blood pH levels, with higher neutrophil counts, CRP, and lactate levels ($P \leq 0.001$), indicating severe inflammatory, hematologic, and metabolic derangement. Neutrophil-to-lymphocyte ratio and bicarbonate levels did not differ significantly, highlighting systemic inflammation and metabolic acidosis as key laboratory features of surgical NEC.

These results were in accordance with **Yu et al.**, **(5)** who observed that neonates requiring surgery had lower WBCs counts, platelet levels, and blood pH ($P < 0.001$), In contrast, CRP, and lactate levels were significantly greater in the surgical group (P below 0.001).

Similarly, in line with **Shang et al.**, **(7)** who found that neonates requiring surgery had lower WBCs counts, (P= 0.000), while, higher CRP (P= 0.002).

Moreover, **Guo et al.**, **(8)** who reported that the values absolute neutrophil count (ANC), (p equal 0.048), and CRP (p equal 0.016) in surgical/death NEC cohort were significantly greater than in the medical NEC cohort.

In contrast with **El Manouni El Hassani et al.**, **(6)** observed that CRP and pH and lactate did not differ significantly between surgical and medical NEC groups.

In the current study, multivariate analysis demonstrated that elevated CRP and lactate levels were independent predictors of operation in newborns with necrotizing enterocolitis, reflecting severe inflammation and tissue hypoperfusion. In contrast, higher white blood cell and absolute lymphocyte counts were protective, indicating that leukopenia and lymphopenia are associated with more severe disease. Lower gestational age also independently predicted the need for surgery, underscoring the vulnerability of preterm infants. These findings highlight the combined impact of inflammatory, metabolic, immunologic, and developmental factors in determining NEC severity.

These results were in accordance with **Yu et al.**, **(5)** who reported that the gestational age ($p = 0.028$) was the independent risk factors for implementing surgical management.

Similarly, it is inconsistent with **Zouari et al.**, **(9)** who assessed predictive factors for surgical management in preterm newborns who had necrotizing enterocolitis in a Tunisian center. Their multivariate logistic analyses illustrated that gestational age 20 mg/L (p equal 0.020, OR equal 2.942) and C-reactive protein level above twenty milligrams per liter (p equal 0.020, OR equal 2.942) have been related to the requirement for surgical management in newborns who had necrotizing enterocolitis.

Moreover, **Tang et al.**, **(10)** who identified independent risk variables related to surgical management in newborns, had necrotizing enterocolitis. They observed that the multivariable analysis demonstrated CRP, serum lactate, diminished absolute lymphocyte count, and white blood cell count as independent predictors of surgery.

Furthermore, **Wang et al.**, **(11)** who determined the utilization value of serum indicators in the selection of surgery opportunities for necrotizing enterocolitis. They revealed that the multivariate logistic regression analysis validated that C-reactive protein was an independent related factor of NEC surgical remedy (P below 0.05).

The obtained findings regarding ROC curve analysis illustrated that CRP had good discriminatory ability for predicting surgical intervention in NEC (AUC = 0.792), with a cut-off value of 19.2 mg/L providing high sensitivity (77%) and specificity (82%). Lactate demonstrated moderate predictive value (AUC = 0.651); although a low cut-off of 1.32 mmol/L yielded high sensitivity (88%), its specificity was limited (37%). These findings suggest that CRP is a more reliable standalone predictor, while lactate may be more useful as a screening marker when combined with other clinical and laboratory parameters.

These results agreed with those of **Jie et al., (12)** who examined the clinical value of intestinal regional oxygen saturation (rSO_2) and CRP in diagnosing necrotizing enterocolitis in preterm babies. The ROC curve study indicated that CRP has an optimum cut-off value of 12.05 milligrams per liter for diagnosing necrotizing enterocolitis in preterm babies, with a sensitivity of 72.7 percent and a specificity of 74.3 percent.

Similarly, in accordance with **Yu et al.**, **(5)** who revealed that the ROC curve analysis illustrated that CRP had an (AUC = 0.792), with optimum cut-off value of 18.5mg/L in the diagnosis of Necrotizing enterocolitis in preterm baby, with a sensitivity of 75%, a specificity of 83%. Lactate demonstrated moderate predictive value (AUC = 0.636); although a low cut-off of 1.250 mmol/L yielded high sensitivity (90%), its specificity was limited (35%).

In contrast with **Shang et al.**, **(7)** who reported that CRP (AUC equal 0.653) had moderate predictive effectiveness, with the optimum cutoff value for expecting surgical timing being 27.515 milligrams per liter for C-reactive protein, and showed poor sensitivity (58.9%) and specificity (71.1%).

CONCLUSION

Prematurity and low birth weight were key baseline risk factors for surgical necrotizing enterocolitis (NEC). Neonates requiring surgery showed more severe clinical signs, advanced Bell's stage, and marked inflammatory and metabolic disturbances. CRP and lactate independently predicted the need for surgery, while higher gestational age, total WBC, and lymphocyte counts were protective. CRP demonstrated good diagnostic accuracy, whereas lactate was highly sensitive but less specific. Overall, integrating demographic factors, clinical severity, and laboratory markers—especially CRP—can permit earlier recognition of high-risk NEC and support timely intervention.

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